In re Application of Christian Rosenmund et al.

Application No.: 09/807,499 Filed: November 5, 2001

Page 2

Attorney Docket No.: VOSS1160

**PATENT** 

## PENDING CLAIMS

- 1. (Original) A nucleic acid molecule encoding a (poly)peptide which has an amino acid sequence of a glutamate receptor of the AMPA-type and/or of a subunit of said receptor and functions as a non-desensitizing AMPA-receptor or as a non-desensitizing subunit thereof, wherein the leucine corresponding to position 497 of the wildtype rat AMPA-receptor GluR1flip or the leucine at the position which corresponds in other glutamate receptors of the AMPA-type by comparison of homology to position 497 of the wildtype rat AMPA-receptor GluR1flip is replaced by an aromatic amino acid.
- 2. (Original) The nucleic acid molecule of claim 1 which is
  - (a) a nucleic acid molecule comprising a nucleic acid molecule encoding the (poly)peptide having the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, or SEQ ID NO: 10, wherein the leucine residue corresponding to position 497 of SEQ ID NO: 1, 5 or 9, corresponding to position 504 of SEQ ID NO: 2, 6 or 10, corresponding to position 507 of SEQ ID NO: 3, to position 505 of SEQ ID NO: 4 or 8, or corresponding to position 513 of SEQ ID NO: 7 is replaced by an aromatic amino acid;
  - (b) a nucleic acid molecule comprising a nucleic acid molecule having the DNA sequence of SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19 or SEQ ID NO: 20, wherein the codon represented by nnn corresponds to a codon coding for an aromatic amino acid;
  - (c) a nucleic acid molecule hybridizing to the complementary strand of a nucleic acid molecule of (a) or (b);

PATENT

Attorney Docket No.: VOSS1160

In re Application of

Christian Rosenmund et al.

Application No.: 09/807,499 Filed: November 5, 2001

Page 3

(d) a nucleic acid molecule being degenerate as a result of the genetic code to the nucleotide sequence of a nucleic acid molecule as defined in (c).

- 3. (Previously Presented) The nucleic acid molecule of claim 1 wherein the (poly)peptide comprises an aromatic amino acid at position 497 of SEQ ID NO:1, 5 or 9, at position 504 of SEQ ID NO: 2, 6, or 10, at position 507 of SEQ ID NO: 3, at position 505 of SEQ ID NO: 4 or 8 or at position 513 of SEQ ID NO: 7, but differs therefrom by at least one mutation selected from the group consisting of amino acid substitutions, addition(s) insertions, deletions, inversions and/or duplications.
- 4. (Previously Presented) The nucleic acid molecule of claim 1 derived from a rat, a mouse or a human.
- 5. (Previously Presented) The nucleic acid molecule of claim 1, wherein said aromatic amino acid residue is tyrosine, phenylalanine, tryptophan or histidine.
- 6. (Previously Presented) The nucleic acid molecule of claim 1 which is DNA, RNA or PNA.
- 7. (Previously Presented) The nucleic acid molecule of claim 1 encoding a fusion protein.
- 8. (Previously Presented) A vector comprising the nucleic acid molecule of claim 1.
- 9. (Original) A vector of claim 8 which is an expression vector, a gene targeting vector and/or a gene transfer vector.
- 10. (Previously Presented) A host transformed with a vector of claim 8 or comprising the nucleic acid of claim 1.

In re Application of PATENT
Christian Rosenmund et al. Attorney Docket No.: VOSS1160

Application No.: 09/807,499 Filed: November 5, 2001

Page 4

11. (Original) The host of claim 10 which is a mammalian cell, an amphibian cell, an insect

cell, a fungal cell, a plant cell or a bacterial cell.

12. (Original) The host of claim 11, wherein said mammalian cell is a HEK cell.

13. (Original) The host of claim 11, wherein said amphibian cell is an oocyte.

14. (Original) The host of claim 13, wherein said oocyte is a frog oocyte.

15. (Original) The host of claim 10 which is a non-human transgenic organism.

16. (Original) The host of claim 15, wherein said non-human organism is a mammal,

amphibian, an insect, a fungus or a plant.

17. (Previously Presented) A method for producing a (poly)peptide encoded by a nucleic acid

molecule of claim 1 comprising culturing a host transformed with a vector containing a nucleic

acid molecule of claim 1 and isolating the produced (poly)peptide.

18. (Previously Presented) A (poly)peptide encoded by the nucleic acid molecule of claim 1.

19. (Original) An antibody specifically directed to the (poly)peptide of claim 18, wherein said

antibody specifically reacts with an epitope comprising the aromatic amino acid which replaces

the leucine at position 497 of the wildtype rat AMPA-receptor GluR1<sub>flip</sub> or the leucine at the

position which corresponds in other glutamate receptors of the AMPA-type by comparison of

homology to position 497 of said wildtype rat AMPA receptor GluR1<sub>flip</sub>.

20. (Original) The antibody of claim 19 which is a monoclonal antibody.

PATENT Attorney Docket No.: VOSS1160

In re Application of Christian Rosenmund et al. Application No.: 09/807,499 Filed: November 5, 2001

Page 5

- 21. (Previously Presented) A composition comprising <u>a</u> nucleic acid molecule of claim 1, a vector of claim 8, a (poly)peptide of claim 18 and/or an antibody of claim 19.
- 22. (Original) The composition of claim 21 which is a pharmaceutical composition, optionally further comprising a pharmaceutically acceptable carrier and/or diluent and/or excipient.
- 23. (Original) The composition of claim 21 which is a diagnostic composition, optionally further comprising suitable means for detection.
- 24. (Original) A method for the blocking of desensitation of glutamate receptor of the AMPA-type, comprising the step of replacing a leucine corresponding to position 497 of the wildtype rat AMPA-receptor GluR1<sub>flip</sub> or the leucine at the position which corresponds in other glutamate receptors of the AMPA-type by comparison of homology to position 497 of the wildtype rat AMPA-receptor GluR1<sub>flip</sub> by an aromatic amino acid.
- 25. (Previously Presented) A method of identifying molecules which are capable of interacting with glutamate receptors of the AMPA-type, comprising the steps of
  - (a) contacting a non-desensitizing AMPA-receptor as encoded by a nucleic acid molecule of claim 1, a vector of claim 8, a host of claim 10, or an antibody of claim 19 with said molecule; and
  - (b) identifying among these molecules the molecules which are capable of interacting with said glutamate receptors of the AMPA-type.
- 26. (Previously Presented) A method for the characterization of molecules which are capable of interaction with glutamate receptors of the AMPA-type, comprising the steps of
  - (a) contacting a non-desensitizing AMPA-receptor as defined in claim 1, a vector of claim 8, a host of claim 10, or an antibody of claim 19 with said molecules; and
  - (b) measuring and/or detecting the characteristic effect said molecules evoke.

PATENT Attorney Docket No.: VOSS1160

In re Application of Christian Rosenmund et al. Application No.: 09/807,499 Filed: November 5, 2001

Page 6

27. (Previously Presented) A method of screening for molecules which are capable of interacting with glutamate receptors of the AMPA-type, comprising the steps of

- (a) contacting a non-desensitizing AMPA-receptor as encoded by a nucleic acid molecule of claim 1, a vector of claim 8 or a host of claim 10 with a candidate molecule; and
- (b) measuring and/or detecting a response; and
- (c) comparing said response to a standard response as measured in the absence of said candidate molecule.
- 28. (Previously Presented) A method for the production of a pharmaceutical composition comprising the steps of the method of claim 25 and comprising a further step, wherein a derivative of said identified, characterized and/or screened molecule is generated.
- 29. (Previously Presented) A method for the production of a pharmaceutical composition comprising the steps of the method of claim 25 and formulating the molecules identified, characterized, screened and/or derivatized in pharmaceutically acceptable form.
- 30. (Previously Presented) The method of claim 25, wherein said molecule(s) comprise(s) (a) neuroprotective and/or (a) nootropic molecule(s).
- 31. (Previously Presented) The method of claim 25, wherein said molecule(s) comprise(s) antagonist(s), partial antagonist(s), partial agonist(s) and/or agonist(s) for glutamate receptors.
- 32. (Previously Presented) Use of a non-desensitizing AMPA-receptor as encoded by the nucleic acid molecule of claim 1 or use of a host as defined in claim 10 as a biosensor for glutamate concentrations.
- 33. (Previously Presented) Use of a non-desensitizing AMPA-receptor as encoded by the nucleic acid molecule of claim 1 or use of a host as defined in claim 10 for the characterization of glutamate receptor channel properties.

In re Application of PATENT
Christian Rosenmund et al. Attorney Docket No.: VOSS1160

Application No.: 09/807,499 Filed: November 5, 2001

Page 7

34. (Previously Presented) Use of a nucleic acid molecule of claim 1, of a vector of claim 8, of a host of claim 10, of a (poly)peptide of claim 18 and/or of the antibody of claim 19 for the preparation of a pharmaceutical composition for preventing and/or treating neurological and/or neurodegenerative disorders.

- 35. (Original) The use of claim 33, wherein said neurological and/or neurodegenerative disorders are selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis (FALS/SALS), ischemia, stroke, epilepsy, AIDS dementia and learning disorders
- 36. (Canceled)
- 37. (Previously Presented) A kit comprising the nucleic acid molecule of claim 1, the vector of claim 8, the host of claim 11, the (poly)peptide of claim 18, the antibody of claim 19 or the molecule as identified, characterized or screened in claim 25.